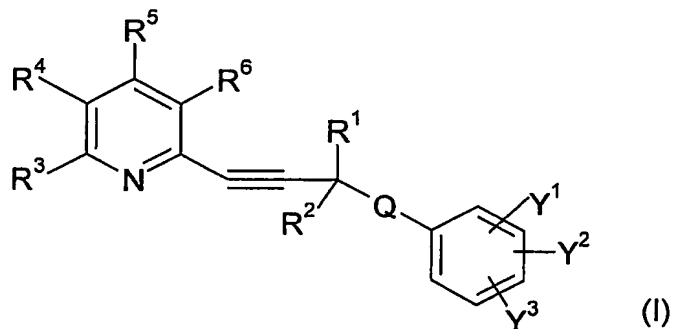


Claims

1. A compound of formula I



wherein

$R^1$  is selected from hydrogen,  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  cycloalkyl, aryl and heteroaryl,  
wherein the aryl or heteroaryl may be substituted by  $C_1$ - $C_4$  alkyl;

$R^2$  is selected from hydrogen and  $C_1$ - $C_4$  alkyl;

$R^3$  is selected from hydrogen,  $C_1$ - $C_4$  alkyl, F,  $CF_3$ ,  $CHF_2$  and  $CH_2F$ ;

$R^4$  is selected from hydrogen, F,  $CF_3$ ,  $CHF_2$ ,  $CH_2F$  and  $CH_3$ ;

$R^5$  is selected from hydrogen and F;

$R^6$  is selected from hydrogen and F;

Q is selected from  $C_1$ - $C_4$  alkyl, optionally substituted by  $C_1$ - $C_4$  alkyl or  $C_1$ - $C_4$  alkoxy;

$Y^1$  is selected from hydrogen; halogen; nitrile;  $C_1$ - $C_4$  alkoxy;  $C_1$ - $C_4$  alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a

fluorine atom; benzyloxy; nitro in the meta or para position; and  $C_1$ - $C_4$  alkyl ester;

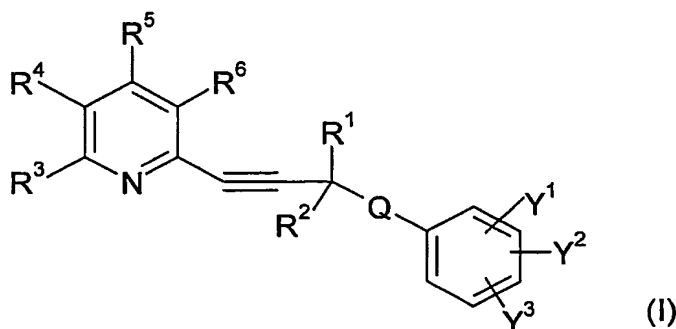
$Y^2$  is selected from hydrogen; halogen; nitrile;  $C_1$ - $C_4$  alkoxy;  $C_1$ - $C_4$  alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom; and  $C_1$ - $C_4$  alkyl ester;

$Y^3$  is selected from hydrogen; halogen; nitrile;  $C_1$ - $C_4$  alkoxy;  $C_1$ - $C_4$  alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom; and  $C_1$ - $C_4$  alkyl ester; or

$Y^1$  and  $Y^2$  may form an aromatic or non-aromatic ring, optionally substituted by halogen, nitrile,  $C_1$ - $C_4$  alkoxy,  $C_1$ - $C_4$  alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom, benzyloxy or  $C_1$ - $C_4$  alkyl ester;

as well as pharmaceutically acceptable salts, hydrates, isoforms and/or optical isomers thereof, with the exception of 4-(4-pyridin-2-yl-but-3-ynyl)-benzonitrile.

## 2. A compound of formula I



wherein

$R^1$  is selected from hydrogen,  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  cycloalkyl, aryl and heteroaryl, wherein the aryl or heteroaryl may be substituted by  $C_1$ - $C_4$  alkyl;

$R^2$  is selected from hydrogen and  $C_1$ - $C_4$  alkyl;

$R^3$  is selected from hydrogen,  $C_1$ - $C_4$  alkyl, F,  $CF_3$ ,  $CHF_2$  and  $CH_2F$ ;

$R^4$  is selected from hydrogen, F,  $CF_3$ ,  $CHF_2$ ,  $CH_2F$  and  $CH_3$ ;

$R^5$  is selected from hydrogen and F;

$R^6$  is selected from hydrogen and F;

Q is selected from  $C_1$ - $C_4$  alkyl, optionally substituted by  $C_1$ - $C_4$  alkyl or  $C_1$ - $C_4$  alkoxy;

Y<sup>1</sup> is selected from hydrogen, halogen, nitrile, C<sub>1</sub>-C<sub>4</sub> alkoxy, and C<sub>1</sub>-C<sub>4</sub> alkyl;  
Y<sup>2</sup> is selected from hydrogen, halogen, nitrile, C<sub>1</sub>-C<sub>4</sub> alkoxy, and C<sub>1</sub>-C<sub>4</sub> alkyl;  
Y<sup>3</sup> is selected from hydrogen, halogen, nitrile, C<sub>1</sub>-C<sub>4</sub> alkoxy, and C<sub>1</sub>-C<sub>4</sub> alkyl;  
as well as pharmaceutically acceptable salts, hydrates, isoforms and/or optical  
isomers thereof, with the exception of 4-(4-pyridin-2-yl-but-3-ynyl)-benzonitrile.

3. A compound according to formula I of claim 1 or 2, wherein

R<sup>1</sup> is hydrogen or C<sub>1</sub>-C<sub>3</sub> alkyl;

R<sup>2</sup> is hydrogen;

R<sup>3</sup> is selected from hydrogen and methyl;

R<sup>4</sup> is hydrogen;

R<sup>5</sup> is hydrogen;

R<sup>6</sup> is hydrogen;

Q is C<sub>1</sub>-C<sub>2</sub> alkyl, optionally substituted by C<sub>1</sub>-C<sub>2</sub> alkyl;

Y<sup>1</sup> is selected from hydrogen, chloro, C<sub>1</sub>-C<sub>2</sub> alkoxy, and C<sub>1</sub>-C<sub>2</sub> alkyl; and

Y<sup>2</sup> is selected from hydrogen, chloro, C<sub>1</sub>-C<sub>2</sub> alkoxy, and C<sub>1</sub>-C<sub>2</sub> alkyl; and

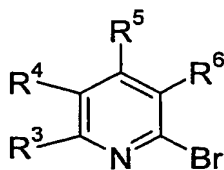
Y<sup>3</sup> is hydrogen.

4. A compound according to claim 1 selected from 2-[4-(3-chlorophenyl)but-1-yn-1-yl]-6-methylpyridine, 2-[4-(3-methoxyphenyl)but-1-yn-1-yl]-6-methylpyridine, 2-methyl-6-[4-(3-methylphenyl)but-1-yn-1-yl]pyridine, 2-methyl-6-(4-phenylbut-1-yn-1-yl)pyridine and 2-methyl-6-(4-phenylpent-1-yn-1-yl)pyridine.

5. A compound according to any one of claims 1-4 for use in therapy.

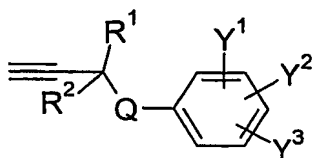
6. A compound according to claim 5, wherein the therapy is treatment or prevention of gastroesophageal reflux disease.

7. Use of a compound according to formula I of claim 1 or 2, or a pharmaceutically acceptable salt or an optical isomer thereof, for the manufacture of a medicament for the inhibition of transient lower esophageal sphincter relaxations.
8. Use of a compound according to formula I of claim 1 or 2, or a pharmaceutically acceptable salt or an optical isomer thereof, for the manufacture of a medicament for treatment or prevention of gastroesophageal reflux disease.
9. Use of 4-(4-pyridin-2-yl-but-3-ynyl)-benzonitrile or a pharmaceutically acceptable salt or an optical isomer thereof, for the manufacture of a medicament for the inhibition of transient lower esophageal sphincter relaxations.
10. Use of 4-(4-pyridin-2-yl-but-3-ynyl)-benzonitrile or a pharmaceutically acceptable salt or an optical isomer thereof, for the manufacture of a medicament for treatment or prevention of gastroesophageal reflux disease.
11. A pharmaceutical composition comprising a compound of formula I of claim 1 or 2 as an active ingredient, together with a pharmacologically and pharmaceutically acceptable carrier.
12. A process for the preparation of a compound of formula I, whereby a coupling reaction of an aryl bromide A



A

and an alkyne B



B

is performed in the presence of a base such as triethyl amine at room temperature to 60 °C, and wherein

$R^1$  is selected from hydrogen,  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  cycloalkyl, aryl and heteroaryl, wherein the aryl or heteroaryl may be substituted by  $C_1$ - $C_4$  alkyl;

$R^2$  is selected from hydrogen and  $C_1$ - $C_4$  alkyl;

$R^3$  is selected from hydrogen,  $C_1$ - $C_4$  alkyl, F,  $CF_3$ ,  $CHF_2$  and  $CH_2F$ ;

$R^4$  is selected from hydrogen, F,  $CF_3$ ,  $CHF_2$ ,  $CH_2F$  and  $CH_3$ ;

$R^5$  is selected from hydrogen and F;

$R^6$  is selected from hydrogen and F;

Q is selected from  $C_1$ - $C_4$  alkyl, optionally substituted by  $C_1$ - $C_4$  alkyl or  $C_1$ - $C_4$  alkoxy;

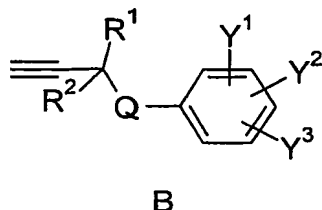
$Y^1$  is selected from hydrogen; halogen; nitrile;  $C_1$ - $C_4$  alkoxy;  $C_1$ - $C_4$  alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom; benzyloxy; nitro in the meta or para position; and  $C_1$ - $C_4$  alkyl ester;

$Y^2$  is selected from hydrogen; halogen; nitrile;  $C_1$ - $C_4$  alkoxy;  $C_1$ - $C_4$  alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom; and  $C_1$ - $C_4$  alkyl ester;

$Y^3$  is selected from hydrogen; halogen; nitrile;  $C_1$ - $C_4$  alkoxy;  $C_1$ - $C_4$  alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom; and  $C_1$ - $C_4$  alkyl ester; or

$Y^1$  and  $Y^2$  may form an aromatic or non-aromatic ring, optionally substituted by halogen, nitrile,  $C_1$ - $C_4$  alkoxy,  $C_1$ - $C_4$  alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom, benzyloxy or  $C_1$ - $C_4$  alkyl ester.

## 13. A compound of formula B



wherein

$R^1$  is selected from hydrogen,  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  cycloalkyl, aryl and heteroaryl, wherein the aryl or heteroaryl may be substituted by  $C_1$ - $C_4$  alkyl;

$R^2$  is selected from hydrogen and  $C_1$ - $C_4$  alkyl;

$R^3$  is selected from hydrogen,  $C_1$ - $C_4$  alkyl, F,  $CF_3$ ,  $CHF_2$  and  $CH_2F$ ;

$R^4$  is selected from hydrogen, F,  $CF_3$ ,  $CHF_2$ ,  $CH_2F$  and  $CH_3$ ;

Q is selected from  $C_1$ - $C_4$  alkyl, optionally substituted by  $C_1$ - $C_4$  alkyl or  $C_1$ - $C_4$  alkoxy;

$Y^1$  is selected from hydrogen; halogen; nitrile;  $C_1$ - $C_4$  alkoxy;  $C_1$ - $C_4$  alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom; benzyloxy; nitro in the meta or para position; and  $C_1$ - $C_4$  alkyl ester;

$Y^2$  is selected from hydrogen; halogen; nitrile;  $C_1$ - $C_4$  alkoxy;  $C_1$ - $C_4$  alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom; and  $C_1$ - $C_4$  alkyl ester;

$Y^3$  is selected from hydrogen; halogen; nitrile;  $C_1$ - $C_4$  alkoxy;  $C_1$ - $C_4$  alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom; and  $C_1$ - $C_4$  alkyl ester; or

$Y^1$  and  $Y^2$  may form an aromatic or non-aromatic ring, optionally substituted by halogen, nitrile,  $C_1$ - $C_4$  alkoxy,  $C_1$ - $C_4$  alkyl wherein one or more of the hydrogen atoms of the alkyl group may be substituted for a fluorine atom, benzyloxy or  $C_1$ - $C_4$  alkyl ester.

14. A compound selected from 1-chloro-3-(4,4-dibromobut-3-en-1-yl)benzene; 1-methoxy-3-(4,4-dibromobut-3-en-1-yl)benzene; 1-methyl-3-(4,4-dibromobut-3-en-

1-yl)benzene; 1-but-3-yn-1-yl-3-chlorobenzene; and (4,4-Dibromo-1-methyl-but-3-enyl)-benzene.

5 15. A method for the inhibition of transient lower esophageal sphincter relaxations whereby an effective amount of a compound of formula I of claim 1 or 2 is administered to a subject in need of such inhibition.

10 16. A method for the treatment or prevention of gastroesophageal reflux disease, whereby an effective amount of a compound of formula I or claim 1 or 2 is administered to a subject in need of such treatment or prevention.